

REMARKS

The instant application is a national filing of PCT patent publication WO 02/068367 (PCT/US02/06339). The application claims priority to three US provisional applications; 60/271,588, 60/271,590, and 60/271,591 all filed on February 26, 2001. New claim 11 is identical to previously presented claim 1 except that the wherein clause d)iii) has been deleted to narrow the scope of this claim. Support for this amendment is found in the specification, page 6, lines 22-25.

The following comments relate to the rejections detailed in the Final Office Action.

Rejection under 35 USC §112 - first paragraph

Claim 1 is rejected under 35 USC §112 - first paragraph in that the claims contain subject matter not described in the specification, specifically, the amendment in claim 1 in the definition of (a).

Support for the amendment in claim 1 (a): "...and: (x) two of R¹, R², R³, and R⁴ are H or (y) R², R³, and R⁴ are H or (z) R¹, R², and R³ are H..." is found in the Specification, page 6, lines 16-18. A copy of the relevant page from the Specification is included in this response for the Examiner's convenience. Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 USC § 102(b)

Claim 1 is rejected under 35 USC § 102(b) as being anticipated by Kostansek, U. S. Patent No. 6,548,448 ("Kostansek") in that Kostansek discloses Benzene, 1-chloro-4-cycloprop-1-enylmethyl. The Examiner indicated in the Final Official Action that this rejection will be withdrawn on the basis of priority, provided that the priority data are corrected by the Applicant.

The priority claim was originally made in a preliminary amendment submitted with the original non-provisional application filing associated with the instant Application. A copy of this preliminary amendment is included with this response for the Examiner's convenience. Unfortunately, it appears that some of the information included in the headings of the preliminary amendment were related to the original provisional filing, which may have led to confusion regarding the priority claim. This Response includes an amendment to the

specification to correct this data. Applicants apologize for any inconvenience this may have caused the Examiner.

Double Patenting - First Rejection (Kostansek)

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Kostansek, U.S. 6,548,448 in that the instant compounds are taught by Kostansek.

Filed with this response is the appropriate terminal disclaimer to overcome this rejection..

Double Patenting - Second Rejection (Lamola et al)

Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-10 Lamola et al, U.S. 6,770,600 ("Lamola") in that the instant compounds are taught by the prior art.

Filed with this response is the appropriate terminal disclaimer to overcome this rejection..

Rejection under 35 USC § 103(a)

Claim 1 is rejected under under 35 USC § 103(a) as being unpatentable over Sisler, E. US Patent No. 6,194,350 ("350"), Daly, et al., US Patent 6,017,849 ("849"), and Minkin, et al., *Theochem, NL*, 1997, 398-399, pp. 237-253 ("Minkin") in that all the references teach cyclopropene derivatives and methods of blocking ethylene receptors in plants.

'350 discloses a method of inhibiting an ethylene response in a plant comprising applying to the plant an effective ethylene response-inhibiting amount of a cyclopropene containing from 1 to 4 R groups wherein each R is independently a C6-C20 alkyl, alkenyl, or alkynyl. '350 further defines "alkyl, alkenyl, and alkynyl" as follows: "...one or more of the carbons in one or more of the R groups is replaced by a group such as ester groups, nitriles, amines, amine salts, acids, acid salts, esters of acids, hydroxyl groups, halogen groups, and heteroatoms selected from the group consisting of oxygen and nitrogen or where such chains include halogen, amino, alkoxy, carboxy, alkoxycarbonyl, oxycarbonylalkyl, or hydroxy substituents." In essence, what this means is that each R group must contain a minimum of six

non-hydrogen atoms which are selected from the group consisting of carbon, oxygen, nitrogen, or halogen. Those substituents of the cyclopropene ring which are not R groups **must** be hydrogen.

'849 discloses encapsulated cyclopropene derivatives in which the cyclopropene is substituted with from 1 to 4 of hydrogen, saturated or unsaturated C1-C4 alkyl, hydroxy, halogen, C1 to C4 alkoxy, amino, and carboxy. The cyclopropene derivatives are the same as those previously disclosed in an earlier patent by Sisler, US Patent No. 5,518,988, which discloses ethylene response antagonistic cyclopropenes substituted with from 1 to 4 of C1 to C4 saturated or unsaturated alkyl, hydroxy, halogen, alkoxy, amino, and carboxy. The difference between '350 and '849 is that '849 teaches encapsulation of the cyclopropenes originally disclosed in Sisler's US Patent No. 5,518,988. Thus, this reference discloses and teaches that certain limited group of small substituents can be effective ethylene antagonists.

'350 is an extension of the disclosure of '849 in that it discloses and teaches ethylene antagonistic cyclopropenes containing from 1 to 4 of C6 to C20 alkyl, alkenyl, and alkynyl groups substituted with a very similar group of substituents as those disclosed in '849. However, the substituent groups again are quite limited in scope. The two references in combination teach that biologically active cyclopropenes can be substituted with a limited number of types of substituents, namely those substituents which contain alkyl, alkenyl, alkynyl, alkoxy, hydroxy, halogen, amino, nitrile, and carboxy. There is no disclosure, teaching, or suggestion in '350 or '849, either alone or in combination, that any other substituent groups would lead to cyclopropenes with ethylene inhibition activity. One of ordinary skill in the art and familiar with these references would note that the cyclopropene substituent groups disclosed in '350 and '849 are not significantly different than those disclosed in the original Sisler patent (US 5,518,988) and, therefore, would conclude that active cyclopropenes must contain only such substituent groups.

Applicants, on the other hand, have discovered that cyclopropenes with ethylene inhibition activity can contain substituent groups, or substituent group patterns, which are significantly different from those disclosed, taught, or suggested by Sisler US 5,518,988, '350, and '849. These very different substituent groups are selected from, a 4 to 14 membered

carbocyclic or heterocyclic ring system; certain silicon, sulfur, phosphorous, or boron-containing groups; and a combination of large and small substituent groups. There is no disclosure, teaching, suggestion, or motivation in '350 or '849, either alone or in combination, that would lead one skilled in the art to Applicants' claimed cyclopropenes. Therefore, the subject matter as a whole of Applicants' claims would not have been obvious to a person having ordinary skill in the art with a knowledge of '350 and '849.

Minkin presents a completely different issue. Minkin relates to computational modeling of the mechanisms of circumambulatory rearrangements of main-group migrants (that is, substituents) in the cyclopropene ring. There is no disclosure, teaching, or suggestion of biological activity of any kind in Minkin. Minkin is concerned with the various mechanistic factors related to substituent group migrations in the cyclopropene ring and comparison of those factors with substituent group migrations in cyclopentadienes. As such, Minkin is clearly non-analogous art. In addition, Minkin does not actually disclose the synthesis of any compound discussed. Rather, the reference is strictly limited to computational modeling of hypothetical compounds (see page 238, Methods). Therefore, Minkin should not be considered as being an enabling reference. However, in order to advance prosecution of this Application, Applicants have now added the dithioformyl group (the substituent in compounds 13a, 13b, 13c, and 13d) to those substituents which are disclaimed (see *In re Johnson and Farnham*, 194 USPQ 187, 196 (1977)).

The compounds specifically noted by the Examiner; that is, compound 2b in scheme 1 on page 239 and compounds 13a, 13b, 13c, and 13d on page 247 are not claimed by Applicants. Compound 2b is a tetrasubstituted cyclopropene (three phenyl groups and an -NCS or -SCN group) whereas Applicants' claimed compounds require at least two hydrogen substituents. Compounds 13 a-d are now disclaimed. In any case, however, due to the non-analogous nature of Minkin, Applicants' compounds would not be obvious to one skilled in the art based upon this reference.

With this response, Applicants believe that the prior rejections have been overcome and the claims are in condition for allowance. Should the Examiner have any suggestions which

may put the Application in better condition for allowance, Applicants' attorney is willing to discuss any such suggestions either by phone or at the U. S. Patent and Trademark Office.

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Typical G groups include, for example: saturated or unsaturated cycloalkyl, bicyclic, tricyclic, polycyclic, saturated or unsaturated heterocyclic, unsubstituted or substituted phenyl, naphthyl, or heteroaryl ring systems such as, for example, cyclopropyl, cyclobutyl, cyclopent-3-en-1-yl, 3-methoxycyclohexan-1-yl, phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-bromophenyl, 3-nitrophenyl, 2-methoxyphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethylphenyl, 2-methyl-3-methoxyphenyl, 2,4-dibromophenyl, 3,5-difluorophenyl, 3,5-dimethylphenyl, 2,4,6-trichlorophenyl, 4-methoxyphenyl, naphthyl, 2-chloronaphthyl, 2,4-dimethoxyphenyl, 4-(trifluoromethyl)phenyl, 2-iodo-4-methylphenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrazinyl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyridazinyl, triazol-1-yl, imidazol-1-yl, thiophen-2-yl, thiophen-3-yl, furan-2-yl, furan-3-yl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, quinolyl, isoquinolyl, tetrahydrofuryl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, morpholinyl, piperazinyl, dioxolanyl, dioxanyl, indolyl and 5-methyl-6-chromanyl, adamantyl, norbornyl, and their substituted analogs such as, for example: 3-butyl-pyridin-2-yl, 4-bromopyridin-2-yl, 5-carboethoxy-pyridin-2-yl, 6-methoxyethoxy-pyridin-2-yl,

Preferably, two of R^1 , R^2 , R^3 , and R^4 are hydrogen. More preferably, R^1 and R^2 are hydrogen or R^3 and R^4 are hydrogen. Even more preferably, R^2 , R^3 , and R^4 are hydrogen or R^1 , R^2 , and R^3 are hydrogen. Most preferably, R^2 , R^3 , and R^4 are hydrogen.

Preferably, n is from 0 to 8. Most preferably, n is from 1 to 7. Preferably, m is 0 to 4. Most preferably, m is from 0 to 2.

Preferably, D1 is -CXY-, -CO-, or -CS-. More preferably D1 is -CXY-.

Preferably, D2 is -O- or -NX-. Preferably, E is -S-, -SiXY-, or -SO₂-. Preferably, X and Y are independently H, halo, OH, SH, -C(O)(C₁-C₄)alkyl-, -C(O)O(C₁-C₄)alkyl-, -O-(C₁-C₄)alkyl-, -S-(C₁-C₄)alkyl, or substituted or unsubstituted (C₁-C₄)alkyl. Preferably, Z is H, halo, or G. More preferably, Z is H or G.

Preferably, each G is independently a substituted or unsubstituted; five, six, or seven membered; aryl, heteroaryl, heterocyclic, or cycloalkyl ring. More preferably, each G is independently a substituted or unsubstituted phenyl, pyridyl, cyclohexyl, cyclopentyl, cycloheptyl, pyrrolyl, furyl, thiophenyl, triazolyl, pyrazolyl, 1,3-dioxolanyl, or morpholinyl. Even more preferably, G is unsubstituted or substituted phenyl, cyclopentyl, cycloheptyl, or cyclohexyl. Most preferably, G is cyclopentyl, cycloheptyl, cyclohexyl, phenyl, or substituted phenyl wherein the substituents are independently selected from 1 to 3 of methyl, methoxy, and halo.